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To cite this version:
Fabrice Galia, Serge Brimioulle, Frederic Bonnier, Nicolas Vandenbergen, Michel Dojat, et al.. Use of maximum end-tidal CO(2) values to improve end-tidal CO(2) monitoring accuracy.. Respiratory Care, Daedalus Enterprises Inc, 2011, 56 (3), pp.278-83. <10.4187/respcare.00837>. <inserm-00635391>
Use of Maximum End-Tidal CO$_2$ Values to Improve End-Tidal CO$_2$ Monitoring Accuracy

Fabrice Galia PhD, Serge Brimioulle MD PhD, Frederic Bonnier, Nicolas Vandenbergen, Michel Dojat PhD, Jean-Louis Vincent MD, and Laurent J Brochard MD

BACKGROUND: The arterial partial pressure of CO$_2$ (P$_{aCO_2}$) can be grossly estimated by the end-tidal partial pressure of CO$_2$ (P$_{ETCO_2}$). This principle is used in SmartCare (Dräger, Lübeck, Germany), which is an automated closed-loop system that uses P$_{ETCO_2}$ to estimate alveolar ventilation during mechanical ventilation. OBJECTIVE: To assess whether the maximum P$_{ETCO_2}$ value (instead of the averaged P$_{ETCO_2}$ value) over 2-min or 5-min periods improves P$_{aCO_2}$ estimation, and determine the consequences for the SmartCare system. METHODS: We continuously monitored breath-by-breath P$_{ETCO_2}$ during ventilation with SmartCare in 36 patients mechanically ventilated for various disorders, including 14 patients with COPD. Data were collected simultaneously from SmartCare recordings, every 2 min or 5 min, and through a dedicated software that recorded ventilation data every 10 s. We compared the maximum and averaged P$_{ETCO_2}$ values over 2-min and 5-min periods to the P$_{aCO_2}$, measured from 80 arterial blood samples clinically indicated in 26 patients. We also compared SmartCare’s classifications of patient ventilatory status based on averaged P$_{ETCO_2}$ values to what the classifications would have been with the maximum P$_{ETCO_2}$ values. RESULTS: Mean P$_{aCO_2}$ was 44 ± 11 mm Hg. P$_{aCO_2}$ was higher than averaged P$_{ETCO_2}$ by 10 ± 6 mm Hg, and this difference was reduced to 6 ± 6 mm Hg with maximum P$_{ETCO_2}$. The results were similar whether patients had COPD or not. Very few aberrant values (< 0.01%) needed to be discarded. Among the 3,137 classifications made by the SmartCare system, 1.6% were changed by using the maximum P$_{ETCO_2}$ value instead of the averaged P$_{ETCO_2}$ value. CONCLUSIONS: Use of maximum P$_{ETCO_2}$ reduces the difference between P$_{aCO_2}$ and P$_{ETCO_2}$, and improves SmartCare’s classification of patient ventilatory status. Key words: alveolar ventilation; capnometry; monitoring; mechanical ventilation; closed loop systems; weaning. [Respir Care 2011;56(3):278–283. © 2011 Daedalus Enterprises]

Introduction

Monitoring of end-tidal partial pressure of CO$_2$ (P$_{ETCO_2}$) has applications in emergency medicine, anesthesia, and intensive care. Although P$_{ETCO_2}$ does not perfectly reflect arterial CO$_2$ measured from an arterial blood sample (P$_{aCO_2}$), capnometry allows continuous monitoring of alveolar ventilation in intubated patients. The SmartCare automated ventilation and weaning system (Dräger, Lübeck, Germany) uses P$_{ETCO_2}$ as a safety parameter, in addition to respiratory rate and tidal volume (V$_T$), to automatically control the pressure-support level. SmartCare averages P$_{ETCO_2}$, respiratory rate, and V$_T$ over 2-min or 5-min periods, classifies the patient’s ventilatory status, and adjusts the pressure-support level accordingly. P$_{ETCO_2}$ is not a main control parameter in SmartCare, but can be used in situations such as a low respiratory rate to help differentiate between, for instance, central hypoventilation leading to hypercapnia versus hyperventilation with hypocapnia. P$_{ETCO_2}$ is known to frequently underestimate P$_{aCO_2}$ because of ventilation-perfusion mismatching and dead-space effect. A spontaneously breathing patient may intermittently have higher P$_{ETCO_2}$ values than the averaged value during prolonged exhalations. Such a value may better reflect alveolar P$_{CO_2}$, and may thus be closer to P$_{aCO_2}$. We assessed the use of the maximum P$_{ETCO_2}$ value instead of the averaged P$_{ETCO_2}$ value over 2 min or 5 min. On the one hand, this could improve the
accuracy of PETCO₂, as a proxy for PaCO₂, and on the other hand it could improve SmartCare’s classifications of the patient’s ventilatory status by using a more reliable PETCO₂ value.

**Methods**

This study was purely observational, and the protocol was approved by the ethics committee of Erasme Hospital, Brussels, Belgium. The study was performed in the Erasme Hospital and Henri Mondor Hospital intensive care units.

**Patients**

The main inclusion criteria were hemodynamic stability, acceptable neurological status (Glasgow coma score ≥ 8), PEEP not higher than 10 cm H₂O, and pressure-support ventilation with pressure support of ≤ 20 cm H₂O. Patients were excluded if a clinical procedure was going to be performed within the next few hours.

**Data Collection**

Arterial blood samples were drawn for clinical indications and analyzed (ABL700, Radiometer, Copenhagen, Denmark, and GEM Premier 4000, Instrumentation Laboratory, Lexington, Kentucky) within a few minutes. Patients were ventilated with an Evita XL ventilator (Dräger, Lübeck, Germany) provided with the SmartCare system and an infrared PETCO₂, mainstream sensor (product number 6871500, Dräger, Lübeck, Germany) connected to a CO₂ cuvette for measurement. During pressure-support ventilation with SmartCare, a dedicated software (VentView, Dräger, Lübeck, Germany) recorded ventilatory data, including PETCO₂, every 10 s. SmartCare averages PETCO₂ values over 2 min or 5 min to classify the patient’s ventilatory status, and we downloaded these data from the ventilator to the computer.

**Procedure**

SmartCare averages respiratory rate, VT, and PETCO₂ over 2 min or 5 min, from values taken at a sampling period of 10 s. The VentView software records the respiratory data at the same sampling period. Recorded data correspond to the last breath of each 10-s data period. In a preliminary study, we compared VentView’s PETCO₂ data averaged along SmartCare periods to SmartCare’s own data, and the difference between VentView and SmartCare’s averaged data was always less than 0.5 mm Hg. For each considered period, the averaged and maximum PETCO₂ were thus determined from the VentView data. Our study of PaCO₂, PETCO₂, and SmartCare concerned 80 SmartCare periods of 2 min or 5 min, during which we took arterial blood samples. We compared SmartCare’s classifications to the maximum PETCO₂ values instead of the averaged PETCO₂ values.

**Statistics**

We analyzed the relationship between PaCO₂ and the averaged and maximum PETCO₂ with linear regression. We used the Pearson test to evaluate the correlation. Quantitative data are expressed as mean ± SD or median and interquartile range.

**Results**

The sample consisted of 36 mechanically ventilated patients, between March 2006 and July 2007. There were 14 females and 22 males, with a mean age of 63 ± 14 y. The patients’ respiratory mechanics, as determined by the ventilator, were: dynamic compliance 44 mL/cm H₂O (IQR 31–63 mL/cm H₂O) and resistance 10 cm H₂O/L/s (IQR 7–13 cm H₂O/L/s). At inclusion, the mean PEEP was 0.40 (IQR 0.31–0.4). Fourteen patients had COPD. Three patients were tracheotomized; the others were orotracheally intubated. All ventilation was with a heated humidifier.

The mean duration of ventilation recordings with SmartCare was 3 hours 36 min per patient (IQR 3 hours 9 min to 4 hours 57 min). Of the 36 subjects, 26 had arterial blood gas measurements contemporaneous with the VentView and SmartCare data.
Relationship Between PETCO₂ and PaCO₂

We analyzed 80 pairs of PETCO₂ and PaCO₂ values from 26 patients. The mean ± SD number of arterial blood gas measurements was 3 ± 1 per patient. Mean PaCO₂ was 44 ± 11 mm Hg.

Table 1 shows the differences between the averaged and maximum PETCO₂ and PaCO₂ values. The pairs of values were obtained during 49 2-min SmartCare periods and 31 5-min SmartCare periods. PaCO₂ was higher than averaged PETCO₂ by 10 ± 6 mm Hg. Taking the maximum instead of the averaged PETCO₂ value reduced the difference with PaCO₂ by 4 mm Hg. Figure 1 shows the linear regression of the averaged and the maximum PETCO₂ against the PaCO₂ values. The coefficient of regression was closer to identity with the maximum PETCO₂ values. Figure 2 plots the maximum PETCO₂ against the averaged PETCO₂.

Relationship Between PETCO₂ and PaCO₂ Relative to COPD

There were 44 values from the 14 COPD patients and 36 values from 12 the non-COPD patients (Table 2). The results were similar whether patients had COPD or not.

Exclusion of PETCO₂ Aberrant Values

We defined an aberrant value as a contextually non-physiologic high PETCO₂ value. Aberrant values, measured via CO₂ infrared sensor, may be due to moisture, water, or dirt on the sensor. Because using one single maximum PETCO₂ value instead of averaged PETCO₂ values ran the risk of using aberrant values, when the difference between 2 consecutive values (separated by 10 s) was more than 40 mm Hg, the latter value was considered aberrant. We found 32 aberrant values (in the 74,777 total measurements), which came from 6 patients. Four patients had only one aberrant value, one patient had 21 aberrant values, and one patient had 7 aberrant values. The rate of aberrant values was 0.04%. We discarded all aberrant values.

SmartCare Classification

The classification of ventilation made by SmartCare for every recording using the averaged PETCO₂ and the maximum PETCO₂ values among the 3,137 SmartCare classifications for the 36 patients differed only for 49 classifications (1.6%), in 9 patients. For the pairs of data related to these classifications, the difference between maximum and averaged PETCO₂ was 16 ± 9 mm Hg, with a median of 13 mm Hg (IQR 13–20 mm Hg).

Discussion

The maximum PETCO₂ value was on average 4 mm Hg closer to PaCO₂ than the averaged PETCO₂. Linear regression between PETCO₂ and PaCO₂ was closer to the identity line with maximum PETCO₂. The use of maximum PETCO₂ in-
frequently changed the classification determined by SmartCare.

**Relationship Between \( P_{ETCO2} \) and \( P_{aCO2} \)**

\( P_{ETCO2} \) is supposed to represent alveolar \( P_{CO2} (P_{ACO2}) \), which is determined by the speeds at which \( CO2 \) is filling alveoli and being emptied from alveoli. The \( P_{ACO2} \) depends on \( CO2 \) production by tissues and venous blood flow content. \( CO2 \) exhalation from alveoli depends on alveolar ventilation. If the alveolar ventilation-perfusion ratio (\( V_A/Q \)) is low, the \( P_{ACO2} \) will be close to venous pressure. If this ratio is normal, the \( P_{ACO2} \) will be close to \( P_{ETCO2} \). If \( V_A/Q \) is high, the \( P_{ACO2} \) will be closer to the inspired \( CO2 \).\(^7\) So \( P_{aCO2} \) tends to be higher than \( P_{ACO2} \), mainly because of ventilation-perfusion discrepancies. \( P_{ACO2} \) and \( P_{ETCO2} \) can thus be different, owing to the patient’s ventilation and pulmonary condition (eg, restrictive or obstructive lung disease). Allowing a prolonged or complete exhalation (compared to a normal breath) could increase \( P_{ETCO2} \).\(^9\) A longer exhalation may therefore better reflect \( P_{ACO2} \) among spontaneous breaths. We inferred that the use of maximum \( P_{ETCO2} \) during periods of 2 min or 5 min, as determined by the SmartCare system for averaging its parameters, could be a better indicator of alveolar ventilation than the averaged \( P_{ETCO2} \) during the same period.

We measured averaged \( P_{ETCO2} \), maximum \( P_{ETCO2} \), and \( P_{aCO2} \) contemporaneously. Table 1 shows that the difference between averaged \( P_{ETCO2} \) and \( P_{aCO2} \) was around 10 mm Hg, a value reported in several previous studies.\(^11-14\) Our maximum \( P_{ETCO2} \) values were closer to \( P_{aCO2} \) by about 4 mm Hg, compared to the averaged \( P_{ETCO2} \). The maximum \( P_{ETCO2} \) had a higher correlation coefficient (\( r = 0.65 \) vs \( 0.57 \)) in all periods (see Fig. 1), which indicates that maximum \( P_{ETCO2} \) better approximates \( P_{aCO2} \) than does averaged \( P_{ETCO2} \).

Maximum \( P_{ETCO2} \) was also found more accurate by Weinger et al.\(^7\) They recorded \( P_{aCO2} \) and \( P_{ETCO2} \) in 25 patients after cardiomyopathy and being weaned with intermit-

### Table 2. \( P_{ETCO2} \) and \( P_{aCO2} \) in COPD Versus Non-COPD Patients During Ventilation With SmartCare

<table>
<thead>
<tr>
<th>Patients</th>
<th>( P_{aCO2} ) (mm Hg)</th>
<th>Averaged ( P_{ETCO2} ) (mm Hg)</th>
<th>Maximum ( P_{ETCO2} ) (mm Hg)</th>
<th>Comparison</th>
<th>Difference (mm Hg) mean ± SD</th>
<th>Pearson Correlation (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without COPD</td>
<td>40 ± 10</td>
<td>31 ± 7</td>
<td>35 ± 9</td>
<td>( P_{aCO2} ) – averaged ( P_{ETCO2} )</td>
<td>9 ± 6</td>
<td>0.773</td>
</tr>
<tr>
<td>(36 paired values, 12 patients)</td>
<td></td>
<td></td>
<td></td>
<td>( P_{aCO2} ) – maximum ( P_{ETCO2} )</td>
<td>5 ± 6</td>
<td>0.813</td>
</tr>
<tr>
<td>With COPD</td>
<td>46 ± 10</td>
<td>35 ± 8</td>
<td>39 ± 7</td>
<td>Maximum ( P_{ETCO2} ) – averaged ( P_{ETCO2} )</td>
<td>4 ± 4</td>
<td>0.936</td>
</tr>
<tr>
<td>(44 paired values, 14 patients)</td>
<td></td>
<td></td>
<td></td>
<td>( P_{aCO2} ) – averaged ( P_{ETCO2} )</td>
<td>11 ± 6</td>
<td>0.799</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>( P_{aCO2} ) – maximum ( P_{ETCO2} )</td>
<td>7 ± 6</td>
<td>0.795</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Maximum ( P_{ETCO2} ) – averaged ( P_{ETCO2} )</td>
<td>4 ± 3</td>
<td>0.903</td>
</tr>
</tbody>
</table>

\( P_{ETCO2} \) = end-tidal partial pressure of \( CO2 \)

**Maximum End-Tidal CO2 Values**

Weinger et al.\(^7\) They recorded \( P_{aCO2} \) and \( P_{ETCO2} \) in 25 patients after cardiomyopathy and being weaned with intermittent mandatory ventilation. \( P_{ETCO2} \) varied widely from breath to breath, and two thirds of the time the \( P_{ETCO2} \) of spontaneous breaths was greater than that of ventilator breaths. Maximum \( P_{ETCO2} \) was the most accurate indicator of \( P_{aCO2} \) (\( r = 0.77, P < .001 \)), and the arterial-to-end-tidal difference was 4 ± 4 mm Hg (\( P < .01 \)).

Chopin et al\(^10\) also found a larger difference between maximum \( P_{ETCO2} \) and \( P_{aCO2} \) in patients with pulmonary embolism (12 mm Hg) versus patients without (1 mm Hg). They used a prolonged passive exhalation until maximum \( P_{ETCO2} \) was reached and found those values much closer to \( P_{aCO2} \).

Lujan et al\(^14\) studied 120 non-ventilated patients and control subjects, classified in 4 equal groups according to COPD severity. With each subject, arterial blood was sampled, then the subject was asked to breathe normally through a mouthpiece attached to a sidestream capnograph, and then to produce 3 maximal exhalations of at least 5 s each. For the entire cohort they found a better Pearson correlation between \( P_{aCO2} \) and \( P_{ETCO2} \) with maximal exhalation (\( r = 0.88, P < .001 \)) than with \( P_{ETCO2} \) during normal tidal breathing (\( r = 0.72, P < .01 \)). However, they also found that \( P_{ETCO2} \) during maximal expiration tended to overestimate \( P_{aCO2} \). In our study we found a similar alveolar- versus-end-tidal \( CO2 \) difference (−2 mm Hg, interquartile range−3 to −1 mm Hg) in only 6 of the 80 pairs of maximum \( P_{ETCO2} \) and \( P_{aCO2} \) values. However, for the whole data the mean difference was positive (6 ± 6 mm Hg). The difference with Lujan’s study,\(^14\) which often found an overestimation of \( P_{aCO2} \) may be due to the long duration of maximal exhalation maneuvers (at least 5 s), while it was only spontaneous exhalations in our study.

**\( P_{ETCO2} \) and \( P_{aCO2} \) Relative to COPD**

\( P_{ETCO2} \) can be a poor proxy for \( P_{aCO2} \) in patients with parenchymal lung disease or emphysema undergoing weaning from mechanical ventilation.\(^15\) In our clinical study we observed (see Table 2) a similar difference (4 mm Hg) between the maximum and averaged \( P_{ETCO2} \) in COPD and

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non-COPD patients. In the non-COPD patients, however, there was a higher correlation coefficient between $P_{\text{aCO}_2}$ and maximum $P_{\text{ETCO}_2}$ ($r = 0.77$ versus $r = 0.81$), whereas the correlation coefficient was not different ($r = 0.8$) in the COPD patients. In both the COPD and non-COPD patients the difference between $P_{\text{ETCO}_2}$ and $P_{\text{aCO}_2}$ was similarly smaller with the maximum $P_{\text{ETCO}_2}$.

We did not measure intrinsic PEEP, which can influence the difference between $P_{\text{aCO}_2}$ and $P_{\text{ETCO}_2}$. Blanch et al.16 addressed this issue in 24 paralyzed and sedated patients on volume-controlled ventilation. They partitioned their population into 2 groups, according to the presence of intrinsic PEEP (13 patients) or not (11 patients). They found a higher $P_{\text{aCO}_2}$/$P_{\text{ETCO}_2}$ difference in the intrinsic PEEP group and a better correlation of $P_{\text{ETCO}_2}$ with $P_{\text{aCO}_2}$ in patients without intrinsic PEEP.

**SmartCare and $P_{\text{ETCO}_2}$**

SmartCare uses $P_{\text{ETCO}_2}$ as a security threshold to delimit the zone of respiratory comfort (Table 3) and in the algorithm by which it classifies the patient’s ventilatory status.17–19 High $P_{\text{ETCO}_2}$ (> 65 mm Hg for COPD, > 55 mm Hg for non-COPD), respiratory rate, and $V_T$ cause SmartCare to classify the ventilation period into a diagnosis such as central hyperventilation, hyperventilation, or insufficient ventilation. Low $P_{\text{ETCO}_2}$ (< 20 mm Hg) is also used to classify unexplained hyperventilation, defined by a high respiratory rate and normal $V_T$ unresponsive to changes in pressure level.19 In SmartCare the use of maximum $P_{\text{ETCO}_2}$ would better classify the patient’s ventilatory status in a very small but potentially important number of cases. Indeed, SmartCare uses different safety thresholds (depending on the presence of chronic CO2 retention, as indicated by the user) to detect central hypoventilation, defined as a low respiratory rate and a high PETCO2 or insufficient ventilation, as a low $V_T$ and a high $P_{\text{ETCO}_2}$. These are rare situations but need to be recognized. If $P_{\text{ETCO}_2}$ markedly underestimates $P_{\text{aCO}_2}$, the diagnosis will occur late (ie, with a very high $P_{\text{aCO}_2}$ value). If at least one $P_{\text{ETCO}_2}$ value during a 2-min or 5-min period is above a $P_{\text{ETCO}_2}$ threshold, it would change SmartCare’s ventilatory status classification. Using the maximum $P_{\text{ETCO}_2}$ would make SmartCare more sensitive to higher CO2 values, which might result in better classification. It could also offer more stability in situations where there is alternation between pathological and non-pathological classifications, because abnormal ventilation would be diagnosed earlier. The use of maximum $P_{\text{ETCO}_2}$ would increase the classifications of hyperventilation and insufficient ventilation, leading SmartCare to increase pressure support or to alarm. The use of maximum $P_{\text{ETCO}_2}$ would have changed 1.6% of the classifications in our patients. There were 28 changes from normal ventilation to insufficient ventilation, which represents 57% of the overall changes in classification. In this study, however, the classification changes were retrospective and did not affect our care decisions.

### Table 3. SmartCare’s Classification of Ventilation Periods*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Spontaneous Respiratory Rate Condition (f)</th>
<th>$V_T$ Condition</th>
<th>$P_{\text{ETCO}_2}$ Condition</th>
<th>Change in Pressure Support</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoventilation</td>
<td>f &lt; f low</td>
<td>$V_T$ low ≤ $V_T$</td>
<td>$P_{\text{ETCO}<em>2}$ high ≤ $P</em>{\text{ETCO}_2}$</td>
<td>Increase</td>
</tr>
<tr>
<td>Acute tachypnea</td>
<td>f max ≤ f</td>
<td>$V_T$ low ≤ $V_T$</td>
<td>20 mm Hg ≤ $P_{\text{ETCO}_2}$</td>
<td>Increase</td>
</tr>
<tr>
<td>Insufficient ventilation</td>
<td>f low ≤ f (&lt; f max)</td>
<td>$V_T$ low ≤ $V_T$</td>
<td>$P_{\text{ETCO}<em>2}$ high ≤ $P</em>{\text{ETCO}_2}$</td>
<td>Increase</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>f high ≤ f (&lt; f max)</td>
<td>$V_T$ low ≤ $V_T$</td>
<td>20 mm Hg ≤ $P_{\text{ETCO}<em>2}$ &lt; $P</em>{\text{ETCO}_2}$ high</td>
<td>Increase</td>
</tr>
<tr>
<td>Central hypotension</td>
<td>f &lt; f low</td>
<td>$V_T$ low ≤ $V_T$</td>
<td>$P_{\text{ETCO}<em>2}$ high ≤ $P</em>{\text{ETCO}_2}$</td>
<td>Increase</td>
</tr>
<tr>
<td>Unexplained hyperventilation</td>
<td>f high ≤ f (&lt; f max)</td>
<td>$V_T$ low ≤ $V_T$</td>
<td>$P_{\text{ETCO}_2}$ &lt; 20 mm Hg</td>
<td>No change</td>
</tr>
<tr>
<td>Normal ventilation</td>
<td>f low ≤ f (&lt; f high)</td>
<td>$V_T$ low ≤ $V_T$</td>
<td>$P_{\text{ETCO}<em>2}$ &lt; $P</em>{\text{ETCO}_2}$ high</td>
<td>Decrease</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>f &lt; f low</td>
<td>NA</td>
<td>$P_{\text{ETCO}<em>2}$ ≤ $P</em>{\text{ETCO}_2}$ high</td>
<td>Decrease</td>
</tr>
</tbody>
</table>

* This table presents all SmartCare diagnosis or classifications functions of different parameters’ values as compared to their threshold. It also presents the consequences on pressure support for each classification. The zone of respiratory comfort corresponds to normal values for the 3 parameters.

$V_T$ = tidal volume (ml)

$P_{\text{ETCO}_2}$ = end-tidal partial pressure of CO2

f low = lower limit of spontaneous breathing frequency: 15 breaths/min

f high = upper limit of spontaneous breathing frequency: 36 breaths/min

$V_T$ low = lower limit of $V_T$: 300 mL (250 mL for body weight < 55 kg)

$V_T$ max = maximum limit of spontaneous breathing frequency: 36 breaths/min

$P_{\text{ETCO}_2}$ high = upper limit of $P_{\text{ETCO}_2}$: 55 mm Hg (65 mm Hg for patients with COPD)

NA = not applicable
Conclusions

Currently, PETCO₂ measurement via infrared sensor usually underestimates PₐCO₂. Maximum PₑTCO₂ seems to be closer to alveolar CO₂ than averaged PETCO₂. Use of maximum PETCO₂ could improve the accuracy and efficiency of SmartCare without being harmful to the patient.

REFERENCES


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